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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,030	09/12/2006	Gianluca Gazza	82062-0169	6978

24633 7590 07/07/2010  
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WASHINGTON, DC 20004

EXAMINER
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BERRIOS, JENNIFER A

ART UNIT	PAPER NUMBER
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1619

NOTIFICATION DATE	DELIVERY MODE
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07/07/2010

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	<b>Application No.</b> 10/552,030	<b>Applicant(s)</b> GAZZA, GIANLUCA	
	<b>Examiner</b> Jennifer A. Berrios	<b>Art Unit</b> 1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 15 January 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,3 and 5-42 is/are pending in the application.
- 4a) Of the above claim(s) 33-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3 and 5-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/10/2010</u> . | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

This Office Action is in response to the reply filed 1/15/2010, wherein claims 2 and 4 have been cancelled and claims 1, 3, 5, 8-10 and 22-32 have been amended.

Currently claims 1, 3, 5-32 are currently being examined and claims 34-42 are withdrawn as being drawn to a non-elected species in the reply filed on 1/16/2009.

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/15/2010 has been entered.

### ***Response to Arguments***

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant argues that sulphated HA and non-sulphated HA are not functional equivalents, as sulfated HA is much more soluble than non-sulfated HA. As such when coated on a medical device, sulfated HA dissolved much more rapidly than non-sulfated HA, therefore one of skill in the art would not be motivated to substitute one for the other. This is not persuasive. As demonstrated in the rejection below, the '741 and '521 patents demonstrate the use of both sulfated and non-sulfated in combination with polymeric materials and therapeutic agents for the preparation of medical and surgical articles. Therefore, one of skill in the art

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would see these as functional equivalents, (which need not have identical properties, but have same function), as they are both ester derivatives of HA used along with medical articles.

Applicant further argues that such substitution by the Examiner is an improper use of hindsight. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant also argues that the '741 patent teaches away from using non-sulfated HA, as it specifically calls for sulfated HA. This is not persuasive. Although the '741 patents preferred/novel embodiment is the use of sulfated HA, it does not discredit, criticize or otherwise discourage the use of non-sulfated HA.

*"Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971)." (see MPEP 2123).*

*Further, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004)." (see MPEP 2141.02).*

Applicant further argues that examiner rejection does not include all the limitations of instant claim 1. Examiner has stated in the office action that US '521 discloses "non-sulfated esters of hyaluronic acid", however no support has been provided for this statement. This is not persuasive. Applicant is directed to the working examples of the '521 patent, wherein it can be seen that the working examples do not have a sulfation step (Examples 22-23 and 25-26, for example).

### **Withdrawn Rejections**

Applicant argument with respect to the rejection of claims 20-23, 25-26 and 28-32 under 35 USC 103 (a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6, 579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), and US 2002/0082679 and US patent 6129956 (issued: 10/10/2000), cited in IDS on 10/3/2005 is persuasive, as such the rejection has been withdrawn. However, a new grounds of rejection is presented below.

### ***Maintained/Modified Rejections***

#### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 3, 5-9, and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6, 579,978 (filed: 4/3/1998) and US Patent 4,851,521 (issued: 7/25/1989).

The '741 patent teaches a coated biomedical object or device having a coating of sulfated polysaccharide, wherein the polysaccharide is a hyaluronic acid, hyaluronate ester or a salt thereof, specifically a sulfated hyaluronate ester (column 16, claims 1 and 4). The '741 patent further teaches that important derivatives of hyaluronic acid are esters thereof with alcohol of the aliphatic, arylaliphatic, heterocyclic and cycloaliphatic series (Column 2, Lines 35-45). US '741 further explain examples of sulfated hyaluronic acid ester that can be used in the present invention. Examples of such include HYAFF 11 (meaning 100% of the carboxyl groups are in the form of benzyl esters) (Column 4, lines 38-43); HYAFF 11p75 (75% benzyl ester of HA) (Column 7, lines 55-58).

US '741 also teaches that pharmaceutical preparations and biomaterials comprising sulfated derivatives of HA can be administered alone or in association with other chemical polymers and/or pharmacologically acceptable drugs (column 14, example 16). Examples include the association of a sulfated HA and a HA ester (non-sulfated) with an antibiotic, anti-inflammatory, antimicrobial, antibacterial and more (Column 15, lines 15-20).

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The '741 patent fails to teach what constitutes a biomedical object or device and also fails to teach the ester derivative of the hyaluronic acid to not be sulfated

The '978 patent teaches biomaterials comprising sulphated hyaluronic acid compounds and derivatives thereof (Claim 1 and 13), wherein the derivative is selected from the group consisting of a partial or total ester (claim 14). The biomaterials can be used to advantage in various fields of surgery, such as in the preparation of cardiac valves and vascular stents (column 5, lines 66-67-column 6, lines 4-5).

The '521 patent teaches non-sulphated esters of hyaluronic acid in which all or only a portion of the carboxylic groups of the acid are esterified and the salts of the partial esters with pharmacologically acceptable organic bases. Pharmaceutical preparation contain a active ingredient, one or more hyaluronic acid esters or a salt there of and a pharmacologically active substance. These can be used in medicine, surgery or cosmetics (Abstract). Alcohols of the aliphathic, araliphathic series can be used as esterifying components of the carboxylic groups of hyaluronic acid. Special attention should be give to benzyl alcohol and phenetyl alcohol (Column 9 lines 25-30 - Column 10 lines 25-37). Of particular interest is those partial esters in which at least 5% and at most 90% of all the carboxylic groups of HY are esterified (Column 9, 39-43).

A vast selection of chemotherapeutic agents can be used for treatment and administered orally or systematically, often in association with steroidal anti-inflammatory agents (Column 12, lines 10-15).

HA may be used as an additive for a wide variety of polymeric materials for use in medical and surgical articles. The addition of HA or one of its salts is effected by covering the surface of such materials, these material can be used for the manufacture of cardiac valves, vascular clips, pacemakers, etc (Column 2, lines 10-20).

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Table 1 of the '521 patent describes 9 HA carboxyl's esterified with corticosteroid. Of these nine, 3 were dissolved in DMSO and the remaining 6 were dissolved in saline. These preparations were administered by instillation in the right eye of rabbits. Results showed that all preparations were effective at reducing inflammation.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to combine the teaching of the '741, '521 patent and the '978 patent. One of ordinary skill in art would have been motivated to substitute a stent for a biomedical object, because it was well known at the time of the invention that stents comprising sulphonated hyaluronic acid compounds and derivatives thereof, are advantages in various fields of surgery, as these compounds have anticoagulant and antithrombotic activities (see Abs. of Patent '978). Furthermore, one of ordinary skill in the art would have been motivated to create medical devices comprising non-sulfated HA ester derivatives as it was well known in the art at the time the invention was made that these could be used in conjunction with polymeric materials and therapeutic agents for the preparation of medical and surgical articles, as demonstrated by patents '741 and '521. One of ordinary skill in the art would have been motivated to substitute two functional equivalents, in this case HA ester derivatives, whether sulfated or non-sulfated, which are taught by the prior art to be useful for the same purpose. Finally one of skill in the art would expect to be reasonable successful because both patents 741 and '521 teach HA ester or salts thereof, whose carboxylic groups are esterified with alcohols selected from aliphatic, arylaliphatic, cycloaliphatic and heterocyclic series.

MPEP 2144.06 recites "*It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.*" *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)."



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The '741 patent also fails to teach the time period for the release of the HA and the active ingredient from the HA polymer coating. As the stent described by the '741 patent has all the structural limitations required by the instant claim 1, it is expected that the properties of the stent of the prior art and that of the instant claims to be the same, absent evidence to the contrary. Therefore the device of the '741 patent would have the same expectancy of release as the stent of instant claim 1.

The above mentioned prior art also fails to teach the thickness of the polymer coating. Since the above art teaches the stent of instant claim 1, it would be obvious to one of ordinary skill to determine the optimum thickness of the HA polymer coating, that would be the most effective.

Therefore claims 1, 3, 5-9, and 16-20 are rejected under 35 USC 103(a) as being unpatentable over the prior art.

6. Claims 11-14 are rejected under 35 USC 103(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6, 579,978 (filed: 4/3/1998) and US Patent 4,851,521 (issued: 7/25/1989), as applied to claims 1, 3, 5-9 and 16-20 above, and further in view of US 2002/0082679 (filing date: 11/1/2001)

US patents '741, '521 and '978 teach the limitation of instant claims 1, 3, 5-9 and 16-20, but fail to teach those limitations further recited by instant claims 11-14.

US 2002/0082679 provide a luminal prosthesis, such as vascular stents and grafts for reducing or inhibiting restenosis (Paragraph 0003). The luminal prosthesis allows for the programmed and controlled substance delivery of therapeutic agents (Paragraph 0028). Therapeutic agents may be selected from a group consisting of immunosuppressants, anti-inflammatory, anti-proliferatives, and anti-migratory agents, among others (Paragraph 0029). It

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also teaches that the source of the therapeutic agent is a polymeric material including therapeutic capable moieties as a structural subunit of the polymer (Paragraph 0031). The prosthesis incorporates the substance by coating the substance on the prosthesis (Pg 21, claim 15). The total amount of the therapeutic agent is generally from .1 micrograms to 10g, but is preferably .1 micrograms to 10mg. This therapeutic agent may be released in a time period, as measured from the time of implanting the device, ranging from 1-200 days, 1-45 days and 7-21 days.

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the polymer and therapeutic coating as taught in US 2002/0082679 for the HA polymer coating and active agent taught in the '741 patent. One of ordinary skill in the art would be motivated to substitute two equivalents, in this case polymers, which are taught by the prior art to be useful for the same purpose, as a medical device coating. Finally, a person of skill in the art would reasonably have expected to be successful because both references disclose biomedical objects comprising a polymer coating that contain an active therapeutic agent.

7. Claims 20-23, 25-26 and 28-32 are rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6, 579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), and US 2002/0082679, as applied to claims 1, 3, 5-9, 11-14 and 16-20 above, (filing date: 11/1/2001) and further in view of US patent 5,759,205 (issued: 6/2/1998)

The US patents '741, '521 and '978 teach the limitations of claims 1, 3, 5-9, 11-14 and 16-20, however fail to teach further limitations set forth by each of claims 21-23, 25-26 and 28-32.

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Claims 21-23 and 32 teach the stent of instant claim 1, further comprising a second coating of a polymer of hydrophobic nature, having a contact angle with water greater than 60°, applied directly to the surface of the stent. Claim 25 further specifies that the polymer of hydrophobic nature is polystyrene. Claims 26, 28 - 30 explain that the hydrophobic polymer, with a thickness of .5-40 micron, preferably 5-10 microns, is associated with an active ingredient (anti-inflammatory, anti-proliferative, anti-migratory and/or immunosuppressant). Said active ingredient is available in quantities between .0001mg and 10mg, and is released over a period of one month. Claim 31 teaches that the active coating of the two polymer coatings can be the same or different.

The '741 and the '521 patent fail to teach whether the coated vascular stents contain one or more coating and the degree of contact with water for the hydrophobic polymer.

The '205 patent discloses implants having improved host tissue ingrowth capability and enhanced blood compatibility comprising at least one tissue-contacting surface of an electrically charged material (Abs). Materials which are useful include polystyrene, FEP, PTFE, PVDF, polylactic acid, etc (Col. 6, lines 55-67). The polymer coating can be applied to the surface of the implant by dipping, spraying and by other methods well known to those of skill in the art (Col. 7, lines 55-60). Example IV demonstrates the use of polystyrene on GRGDS/HYAFF (ester derivative of HA). Cell attachment levels were greater on samples comprising polystyrene.

The contact degree with water of polystyrene although not specifically stated can be expected to have the same properties as disclosed by the applicant since the polymers are equivalent to one another.

The above mentioned prior art also fails to teach the thickness of the polymer coating. Since the above art teaches the stent of instant claim 1 with the limitations of claim 21, it

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would've been *prima facie* obvious to one of ordinary skill at the time the invention was made to determine the optimum thickness of the HA polymer coating that would be the most effective.

US 2002/0082679 teaches polymeric material on a stent containing therapeutic agents. US '741 teaches a stent with HA polymer coating which can additionally contain active agents and the '205 patent teaches an object having enhanced cell adhesion which comprises a polymeric material coating (polystyrene) in combination with HA, although no mention of therapeutic agents are made. However as taught above in US 2002/0082679 the source of the therapeutic agents associated with vascular stent coatings are polymers.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the teaching of US 2002/0082679, the '741 and '521 patent and the '205 patent since both the '741 patent and the '205 patent teaches medical devices coated with polymers in combination with esterified HA and the '741 patent, further more the '205 patent teaches that the use of polystyrene results additional benefits, such as enhanced cell adhesion, and the '741 patent teaches that these polymers can comprise therapeutic agents. It would be obvious to one of ordinary skill, as these two compositions are taught by the prior art to be useful for the same purpose and therefore it would be obvious to combine the two to form a third composition for the same purpose.

8. Claim 24 is rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6, 579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), US 2002/0082679 (filing date: 11/1/2001) and US patent (5,759,205, issued: 6/2/1998), as applied to claims 1, 3, 5-9, 11-14, 16-23, 25-26 and 28-32 above, and further in view of Vercruysse (Critical Reviews in Therapeutic Drug Carrier Systems, 1998).

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The US patents '741, '521, '978 and '959 teach the limitations of claim 24, however they fail to teach a further limitation set forth by the claim. Claim 24 further teaches the second coating of the stent of instant claim 21 to be polymethyl methacrylate among others, with a contact degree angle with water of 60°. The above teachings fail to specify one of the exact polymers given in claim 24. The above art teaches a polystyrene coated with HA and derivatives there of, while Vercruysse specifically teaches polymethyl methacrylate coated with HA (pg 528, lines 5-9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute polystyrene for polymethyl methacrylate since the prior art teaches these to be equivalents, both hydrophobic and both are coated with HA. The contact degree with water of polystyrene although not specifically stated can be expected to have the same properties as disclosed by the applicant since the polymers can be considered equivalents to one another.

9. Claims 10 and 15 are rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6, 579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), and US 2002/0082679, (filing date: 11/1/2001) as applied to claims 1, 3, 5-9, 11-14 and 16-20 above, and further in view of WO 99/03854 (pub date: 1/28/1999, cited on the 10/3/2005 IDS).

The US patents '741, '521 and '978 and the '679 publication teach the limitations of claims 10 and 15, however fail to teach further limitations set forth by each claim. Claims 10 and 15 further teach that the active agent associated with the stent of instant claim one is specifically 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

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US 2002/0082679 and the '741 and '521 patent teach the stent of instant claim 1 with an active agent, with quantities preferably of .1 micrograms to 10mg. What they fail to teach is the active ingredient being 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

WO 99/03854 teaches that 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate is effective in diseases associated with vascular smooth-muscle migration and proliferation, such as restenosis and atherosclerosis (pg 12, lines 25-27). As such 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate can thus inhibit proliferation and especially the migration of vascular smooth-muscle cells (pg 16, lines 1-3).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of WO 99/03854 with US 2002/0082679 and the '741, '521 and the '978 patents as it was well known at the time of the invention, the properties of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate and it would be obvious to use this compound as an active agent in a medical stent to treat restenosis with a reasonable expectation of success.

10. Claim 27 is rejected under 35 USC 130(a) as being unpatentable over US patent 6,027,741 (issued 2/22/2000), cited in IDS on 10/3/2005, US patent 6, 579,978 (filed: 4/3/1998), US Patent 4,851,521 (issued: 7/25/1989), and US 2002/0082679 (filing date: 11/1/2001) and US patent (5,759,205, issued: 6/2/1998), as applied to claims 1, 6-9, 11-14, 16-23, 25-26 and 28-32 above, and further in view of WO 99/03854 (pub date: 1/28/1999).

The US patents '741, '521 and '978 and '956 and the '679 publication teach the limitations of claim 27, however fail to teach the further limitations set forth the claim. Claim 27

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further teaches that the active agent associated with the stent of instant claim 21 is specifically 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate.

The above teaching fails to teach this exact active ingredient as the therapeutic agent. WO 99/03854 teaches that 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate is effective in diseases associated with vascular smooth-muscle migration and proliferation, such as restenosis and atherosclerosis (pg 12, lines 25-27). As such 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate can thus inhibit proliferation and especially the migration of vascular smooth-muscle cells (pg 16, lines 1-3).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of US patents '741, '521 and '978 and '956 and the '679 publication with WO 99/03854 as it was well known at the time of the invention the properties of 4-[(4-methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]animo]-phenyl] benzamide methane sulphonate and it would be obvious to use this compound as an active agent in a medical stent to treat restenosis.

### **Conclusion**

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer A. Berríos whose telephone number is (571)270-7679. The examiner can normally be reached on Monday-Thursday: 7:00am-4:00pm (EST).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 270-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer A Berríos/  
Examiner, Art Unit 1619

/Tracy Vivlemore/  
Primary Examiner, Art Unit 1635